with progression and cartilage loss in OA using MRI. Studies have been performed under non-weight-bearing (NWB) conditions, and little is known about alterations of the meniscus under weight-bearing (WB) conditions. It has also been suggested that meniscal extrusion may cause joint space narrowing (JSN) in WB radiographs, but radiography is unable to delineate the meniscus directly. The purpose of this study was therefore to use MRI to investigate the impact of WB conditions on the shape, position and signal of the medial meniscus (MM).

Methods: One knee in each of 26 women (age 55±5.6 years; BMI 27.9±2.3 kg/m^2) was studied; 9 were healthy (Kellgren Lawrence grade [KLG] 0) and 17 had radiographic evidence of OA (10 KLG 2; 7 KLG 3). 3 Tesla MR images were acquired using a T2-weighted fat-suppressed coronal FSE sequence (2×0.31×0.31 mm). Images were acquired with the participant supine, first under NWB and then under simulated WB conditions, applying a force of 50% body weight to the lower extremities. Manual segmentation of the tibial, femoral and external surfaces of MM, and of the tibial joint surface area was performed by one reader (RF) and quality controlled by another (FE). Both readers were blinded to KLG and WB/NWB status. Measures were computed for the entire MM and for the anterior/posterior horns and the middle portion, using custom software (Chondrometrics GmbH, Ainring, Germany). Differences between WB and NWB conditions were assessed using the Wilcoxon signed rank test, and differences (in differences between WB and NBW) between OA and healthy knees using the Mann Whitney U-test.

Results: There was no significant difference in the volume (p=0.89) and mean or maximal thickness (p=0.81/p=0.09) of the whole MM between WB and NWB. The external surface, however, displayed increased bulging under WB (median 0.30 vs. 0.25 mm; p=0.03). In the middle portion of MM, the maximal thickness INcreased from 6.8 to 7.3 mm (p=0.02) and the bulging was 0.31 vs. 0.23 mm (p=0.01) under WB. Extrusion significantly increased under WB: the tibial area covered by MM decreased from 38% to 36% ($p<0.001$), the external MM surface was located 2.31 vs. 2.00 mm medial to the margin of the tibial surface (p=0.01), and the intersection of the tibial and femoral MM surface was located 3.5 mm vs. 3.9 mm lateral to the margin of the tibial surface (p=0.006). In the middle portion, the position of the external MM surface was 2.47 vs. 2.02 mm medial to the margin of the tibial surface (p=0.002). The signal intensity of the entire meniscus increased under WB conditions (p=0.001). This was also observed in the anterior/posterior horns and in the middle portion of the MM ($p\leq0.001$). Differences in extrusion between WB and NWB were greater in OA than in healthy knees (p=0.034 for location of the external MM surface).

Conclusions: In this first quantitative in vivo study we find that MM extrusion significantly increased under WB conditions; differences between WB and NWB conditions were stronger in OA versus healthy knees. The signal in the MM also significantly increased under WB, potentially due to alterations in collagen structure. However, the volume and mean thickness of MM did not differ between WB and NWB. Surprisingly, the maximal thickness of the middle portion (measured at the external margin of MM) significantly increased during WB. Futures studies will look at the relative contribution of meniscal extrusion and cartilage deformation to JSN.

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CLINICAL AND ULTRASONOGRAPHIC PREDICTORS OF JOINT REPLACEMENT FOR KNEE OSTEOARTHRITIS: RESULTS FROM A LARGE, 5 YEARS, PROSPECTIVE EULAR STUDY

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Purpose: To determine clinical and ultrasonographic predictors of joint replacement surgery across Europe in primary osteoarthritis (OA) of the knee.

Methods: This was a 5-year prospective study of a painful OA knee cohort (from a EULAR-sponsored, multi-center study). All subjects had clinical evaluation, radiographs and ultrasonography (US) at study entry. The rate of knee replacement surgery over the 5-year follow-up period was determined using Kaplan-Meier survival data analyses. Predictive factors for joint replacement were identified by univariate Log-rank test then multivariate analysis using a Cox proportional-hazards regression model. Potential baseline predictors included demographic, clinical, radiographic and US features.

Results: Of the 600 original patients, 531 (88.5%), mean age 67±10 years, mean disease duration 6.1±6.9 years had follow-up data and were analyzed. During follow-up, knee replacement was done or required for 131 patients (survival rate estimation of 72.2%). By multivariate analysis, predictors of articular replacement were: Kellgren & Lawrence radiographic grade (grade $\geq$ III-IV versus $<$ III, Hazards Ratio (HR) = 3.00 [95% CI = 1.91-4.70], $p<0.0001$); ultrasonographic knee effusion or ultrasonographic knee synovitis (ultrasonographic knee effusion depth or ultrasonographic knee synovitis versus none, HR = 2.51 [95% CI = 1.69-3.74], $p<0.0001$); WOMAC pain subscale ($\geq$ 50 versus $<$50, HR = 1.77 [95% CI = 1.18-2.67], p=0.0058); and disease duration ($\geq$ 5 years versus $<$5 yrs, HR= 1.76 [95% CI=1.20-2.58], p=0.0039).

Conclusions: Longitudinal evaluation of this OA cohort demonstrated significant progression to joint replacement. In addition to severity of radiographic damage and pain, US detected effusion or US synovitis were a predictor of subsequent joint replacement.

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THE EFFECTS OF THIRD METACARPAL GEOMETRY ON THE INCIDENCE OF CONDYLAR FRACTURES IN THOROUGHBRED RACEHORSES

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Purpose: The objective of this study was to determine the influence of third metacarpal surface geometry on third metacarpal condylar fracture in Thoroughbred racehorses.

Methods: Computed tomographic scans of horses with condylar fractures (n=51, FX) the contralateral limbs of the same horses (n=51, NFX) and non-fractured horses (n=80, CTL) were made. The images were rendered into three dimensional image of the condylar surface in order to characterize condylar width, condylar

area, and radius of curvature in the joints. A mixed model analysis of variance was used to compare data between the three different groups.
Results: Radius of curvature varied significantly between the FX and CTL groups at five sites and in particular was more strikingly different in the lateral condyle near the parasagittal groove. In addition the ratio of lateral to medial condylar width was significantly different between the FX and CTL groups at eight of nine sites and in the NFX and CTL groups at two sites. In particular the lateral condyle was relatively smaller compared to the medial condyle in FX horses.
Conclusions: It appears that in horses with condylar fracture, their lateral condyle was significantly smaller compared to their medial condyles when compared to non-fractured horses. In addition the radius of curvature was significantly different in fractured horses compared to non-fractured horses. These differences in geometrical properties may possibly be used for a screening tool in the future

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A MICROARRAY ANALYSIS OF DAMAGED VERSUS UNDAMAGED CARTILAGE IN ANTEROMEDIAL GONARTHROSIS

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Purpose: Anteromedial gonarthrosis (AMG) is a distinct phenotype of osteoarthritis (OA), with a specific pattern of disease. There is full thickness cartilage loss anteromedially, progressing to an area of damaged cartilage, and then to an area of macroscopically and histologically normal cartilage posteriorly. It can be considered to be a spatial model of OA progression and used to study the progression of cartilage degeneration. Gene expression differences between regions have previously been shown and microarray technology presents the opportunity to compare the gene expression of tens of thousands of genes. To date microarray has been used sparingly in OA.
Methods: Ten tibial resection specimens were obtained from patients undergoing unicompartmental knee arthroplasty. The edges of cartilage were excluded, and regions of damaged and undamaged cartilage were dissected from underlying bone. The samples were divided into two equal amounts, and "mirror" samples kept back for real time Polymerase chain reaction (qPCR) validation. Samples were hand ground under liquid nitrogen and RNA extracted using RNeasy kits. The RNA was reverse transcribed and quality control undertaken using a bioanalyser. Each pair of samples was labelled using Agilent's two-colour microarray-based gene expression analysis protocol and run on a whole genome microarray plate.
Results: Bioanalyser data showed adequate quantity and quality: the average RNA integrity number (RIN) was 7.3 (range 6.5 - 8.1). Initial analysis revealed 820 genes that were significantly up- (416) or down- (404) regulated in damaged cartilage, with at least a 2-fold change.
A search for differences in gene ontologies (GO) showed significant functional clusters in groups including, cell communication, collagen process and proteinaceous extracellular matrix. There was an increase in undamaged cartilage of Type I Collagen expression (validated with qPCR). There was a decrease in several Matrix metalloproteinase (MMP) expression in damaged cartilage, the most downregulated being MMPs 1, 2, 3, 9, and 13. There was also decreased expression of the Wnt antagonists FRZB (which has shown genetic association with OA), sFRP1 and sFRP4 and increased expression of the BMP antagonist Noggin in damaged compared to undamaged cartilage.
Conclusions: This study has generated results showing a number of changes in gene expression that warrant further investigation. In terms of matrix changes, Type I collagen content has been shown previously to be increased in the undamaged cartilage of AMG using immunoassays. The MMP results were somewhat unexpected, but raises potential questions regarding where OA cartilage samples are obtained from in cellular studies. Furthermore, in AMG the signalling microenvironment is altered, and results implicate both Wnt and BMP signaling in regulation of cartilage damage. Further validation of selected genes is ongoing, and ultimate aims are to identify a series of therapeutic targets for disease modifying interventions.

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A NOVEL WHOLE-TISSUE MODEL FOR DRUG SCREENING REVEALS THE IMPORTANCE OF CELL COMMUNICATION BETWEEN SUBCHONDRAL BONE AND CARTILAGE IN THE PATHOGENESIS OF OSTEOARTHRITIS

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Purpose: The pathophysiology of osteoarthritis (OA) involves the whole joint, and is characterized both by cartilage degradation and altered subchondral bone turnover. However, which of these tissues initiates the pathogenesis of OA and which are the drivers of the disease, is of high interest to understand the aetiology of OA. At present there are neither biological models nor tools that allow investigation of the interactions between osteoblasts, osteoclasts and chondrocytes in one whole tissue system *in vitro*. Thus, we developed and characterised an *ex vivo* murine femoral head model, enabling us to investigate cell interactions between bone- and cartilage-tissue and test novel drug candidates for osteoarthritis.
Methods: Femoral heads from three, six, nine and twelve weeks old mice were isolated and cultured for 10 days in serum-free media (DMEM:F12) in absence (control) or presence of IGF-I [100 nM] (anabolic conditions), oncostatin M (OSM) [10 ng/mL] + TNF-α [20 ng/mL] (catabolic conditions) or PTH [1, 10 and 100 nM]. The conditioned medium was kept for analysis of biochemical markers of bone and cartilage turnover, including CTX-I (bone resorption), CTX-II (cartilage degradation), PIINP (cartilage formation), Hydroxyproline (collagen release), TRACP (osteoclast number), and GAG release (proteoglycan turnover). Viability or overall living cell numbers of the femoral heads was monitored using the dye Alamar Blue, after 10 days of culture. Passive release from metabolically inactive femoral heads was measured as background. Microscopic changes were assessed by histology.
Results: Cell viability was increased upon anabolic and catabolic stimulation at day 10. Stimulation with the cytokines OSM + TNF-α resulted in an increased bone resorption, cartilage degradation, collagen release, proteoglycan turnover and number of osteoclasts, measured by specific biomarkers in the conditioned media. Stimulation with IGF-I decreased the osteoclast number. Cartilage formation increased when stimulated with IGF-I, whereas it decreased when stimulated with OSM + TNF-α, but only in three weeks old mice. PTH dose dependently increased the osteoclast number and bone resorption. Highest dose of PTH increased cartilage formation, cartilage degradation and collagen release, indicating a dual action of PTH in this whole tissue model.
Histological examinations of the femoral heads showed a ratio in bone vs cartilage increasing with age, probably due to the initiating secondary ossification centre in femoral heads from nine weeks old mice.